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SEQUENCE LISTING

<110> Anderson, John P.

Basi, Guriqbal

Doane, Minh Tam

Frigon, Normand

John, Varghese

Power, Michael

Sinha, Sukanto

Tatsuno, Gwen

Tung, Jay

Wang, Shuwen

McConlogue, Lisa

<120> Beta-Secretase Enzyme Compositions and Methods

<130> 228-US-NEW

<140> US 09/471,669

<141> 1999-12-24

<150> 60/114,408

<151> 1998-12-31

<150> 60/119,571

<151> 1999-02-10

<150> 60/139,172

<151> 1999-06-15

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 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val ✓  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr ✓  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr ✓  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val ✓  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320

  
 Val  
 ca don

GTG

Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
325 330 335  
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
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Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
355 360 365  
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
370 375 380  
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
385 390 395 400  
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
405 410 415  
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
420 425 430  
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435 440 445  
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
450 455 460  
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
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<212> DNA

<213> Artificial Sequence

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<211> 23

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ID NO: 2

  
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agagacgarg arccsgaaga gcc

23

<210> 9

<211> 23

<212> DNA

<213> Artificial Sequence

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ID NO: 2

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23

<210> 10

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ID NO: 2

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<400> 18  
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<210> 21

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ID NO: 2

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<221> misc\_feature

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<210> 23

<211> 17

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<210> 29

<211> 17

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<223> Degenerate oligonucleotide primer

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<222> (1) ... (17)

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35 40 45  
Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
50 55 60  
His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
65 70 75 80  
Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
85 90 95  
Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
100 105 110  
Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
115 120 125  
Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
130 135 140  
Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
145 150 155 160  
His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
165 170 175  
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
180 185 190  
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
195 200 205  
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
210 215 220  
Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
225 230 235 240  
Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
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 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
 325 330 335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
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 355 360 365  
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala  
 370 375 380  
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr  
 385 390 395 400  
 Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val  
 405 410 415  
 Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val  
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<210> 49

<211> 32

<212> DNA

<213> Homo sapiens

<400> 49

cccgccgga gggcagctt tgtggagatg gt 32

<210> 50

<211> 11

<212> PRT

<213> Homo sapiens

<400> 50

Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val

1

5

10

<210> 51

<211> 5

<212> PRT

<213> Homo sapiens

<400> 51

Val Asn Leu Asp Ala

1

5

<210> 52

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic oligopeptide substrate

<400> 52

Ser Glu Val Asn Leu Asp Ala Glu Phe

1

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<210> 53

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic oligopeptide substrate

<400> 53

Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile

1

5

10

15

Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe

20

25

30

<210> 54

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<223> Wild type Amyloid Precursor Protein cleavage site  
(fragment)

<400> 54

Val Lys Met Asp Ala

1

5

<210> 55

<211> 24

<212> PRT

<213> Homo sapiens

<400> 55

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10 15  
Glu Met Val Asp Asn Leu Arg Gly  
20

<210> 56  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 56  
Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg  
1 5 10 15

<210> 57  
<211> 419  
<212> PRT  
<213> Homo sapiens

<400> 57  
Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
1 5 10 15  
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
20 25 30  
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
35 40 45  
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
50 55 60  
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
65 70 75 80  
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
85 90 95  
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
100 105 110  
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
115 120 125  
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
145 150 155 160  
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
165 170 175  
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
180 185 190  
Ser Leu Glu Pro Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
195 200 205  
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
210 215 220  
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
225 230 235 240  
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
245 250 255  
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
260 265 270  
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
275 280 285  
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
290 295 300  
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
305 310 315 320  
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
325 330 335  
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
340 345 350  
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
355 360 365  
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
370 375 380  
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
385 390 395 400  
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
405 410 415  
Val Ser Ala

<211> 407

<212> PRT

<213> Homo sapiens

<400> 58

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10 15  
Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
20 25 30  
Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
35 40 45  
Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
50 55 60  
His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
65 70 75 80  
Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
85 90 95  
Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
100 105 110  
Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
115 120 125  
Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
130 135 140  
Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
145 150 155 160  
His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
165 170 175  
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
180 185 190  
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
195 200 205  
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
210 215 220  
Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
225 230 235 240  
Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
245 250 255  
Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys

260	265	270
Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala		
275	280	285
Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met		
290	295	300
Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln		
305	310	315
Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr		
325	330	335
Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val		
340	345	350
Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile		
355	360	365
Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala		
370	375	380
Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr		
385	390	395
Asn Ile Pro Gln Thr Asp Glu		
405		

<210> 59

<211> 452

<212> PRT

<213> Homo sapiens

<400> 59

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val		
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser		
20	25	30
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp		
35	40	45
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val		
50	55	60
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr		
65	70	75
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser		
85	90	95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
100 105 110  
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
115 120 125  
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
130 135 140  
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
145 150 155 160  
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
165 170 175  
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
180 185 190  
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
195 200 205  
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
210 215 220  
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
225 230 235 240  
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
245 250 255  
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
260 265 270  
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
275 280 285  
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
290 295 300  
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
305 310 315 320  
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
325 330 335  
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
340 345 350  
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
355 360 365  
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
370 375 380  
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
385 390 395 400

Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
405 410 415  
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
420 425 430  
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
435 440 445  
Gln Thr Asp Glu  
450

<210> 60  
<211> 420  
<212> PRT  
<213> Homo sapiens

<400> 60  
Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
1 5 10 15  
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
20 25 30  
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
35 40 45  
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
50 55 60  
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
65 70 75 80  
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
85 90 95  
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
100 105 110  
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
115 120 125  
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
130 135 140  
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
145 150 155 160  
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
165 170 175  
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp

180	185	190
Ser Leu Glu Pro Phe Asp Ser Leu Val Lys Gln Thr His Val Pro		
195	200	205
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln		
210	215	220
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile		
225	230	235
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg		
245	250	255
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln		
260	265	270
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val		
275	280	285
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala		
290	295	300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp		
305	310	315
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr		
325	330	335
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val		
340	345	350
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg		
355	360	365
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala		
370	375	380
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu		
385	390	395
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala		
405	410	415
Val Ser Ala Cys		
420		

<210> 61  
 <211> 8  
 <212> PRT  
 <213> Artificial Sequence

<220>

<223> Synthetic peptide inhibitor

<221> MOD\_RES

<222> 4

<223> Xaa = hydroxyethylene

<400> 61

Glu Val Met Xaa Val Ala Glu Phe

1 5

<210> 62

<211> 26

<212> PRT

<213> Homo sapiens

<400> 62

Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met

1 5 10 15

Leu Pro Leu Cys Leu Met Val Cys Gln Trp

20 25

<210> 63

<211> 33

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P4'sw peptide substrate

<400> 63

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu

1 5 10 15

Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu

20 25 30

Phe

<210> 64

<211> 29

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P1' peptide substrate with CGG linker

<400> 64

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu

1 5 10 15

Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu

20 25

<210> 65

<211> 501

<212> PRT

<213> Mus musculus

<400> 65

Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met

1 5 10 15

Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser

20 25 30

Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp

35 40 45

Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val

50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr

65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser

85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr

100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val

115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp

130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile

145	150	155	160
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp			
165	170	175	
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp			
180	185	190	
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro			
195	200	205	
Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln			
210	215	220	
Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile			
225	230	235	240
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg			
245	250	255	
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln			
260	265	270	
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val			
275	280	285	
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala			
290	295	300	
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp			
305	310	315	320
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr			
325	330	335	
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val			
340	345	350	
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg			
355	360	365	
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala			
370	375	380	
Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu			
385	390	395	400
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala			
405	410	415	
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu			
420	425	430	
Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro			
435	440	445	
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala			

450 455 460  
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
465 470 475 480  
Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp  
485 490 495  
Ile Ser Leu Leu Lys  
500

<210> 66  
<211> 480  
<212> PRT  
<213> Homo sapiens

<400> 66  
Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
1 5 10 15  
Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
20 25 30  
Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
35 40 45  
Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
50 55 60  
Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
65 70 75 80  
Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu  
85 90 95  
Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr  
100 105 110  
Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro  
115 120 125  
His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu  
130 135 140  
Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly  
145 150 155 160  
Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe  
165 170 175  
Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu  
180 185 190

Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala  
195 200 205  
Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr  
210 215 220  
Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu  
225 230 235 240  
Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp  
245 250 255  
Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr  
260 265 270  
Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile  
275 280 285  
Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly  
290 295 300  
Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe  
305 310 315 320  
Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe  
325 330 335  
Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val  
340 345 350  
Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser  
355 360 365  
Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val  
370 375 380  
Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His  
385 390 395 400  
Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr  
405 410 415  
Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser  
420 425 430  
Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe  
435 440 445  
Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys  
450 455 460  
Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys  
465 470 475 480

<211> 444

<212> PRT

<213> Homo sapiens

<400> 67

Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
1 5 10 15  
Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
20 25 30  
Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
35 40 45  
His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
50 55 60  
Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
65 70 75 80  
Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
85 90 95  
Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
100 105 110  
Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
115 120 125  
Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
130 135 140  
Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
145 150 155 160  
Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
165 170 175  
Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
180 185 190  
Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
195 200 205  
Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
210 215 220  
Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
225 230 235 240  
Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
245 250 255  
Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val

260	265	270
Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser		
275	280	285
Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile		
290	295	300
Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln		
305	310	315
Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val		
325	330	335
Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala		
340	345	350
Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu		
355	360	365
Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu		
370	375	380
Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr		
385	390	395
Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu		
405	410	415
Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln		
420	425	430
His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys		
435	440	

<210> 68  
 <211> 395  
 <212> PRT  
 <213> Homo sapiens

<400> 68			
Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln			
1	5	10	15
Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn			
20	25	30	
Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro			
35	40	45	
His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr			
50	55	60	

Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
65 70 75 80  
Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
85 90 95  
Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
100 105 110  
Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
115 120 125  
Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
130 135 140  
Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
145 150 155 160  
Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
165 170 175  
Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
180 185 190  
Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
195 200 205  
Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
210 215 220  
Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
225 230 235 240  
Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
245 250 255  
Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
260 265 270  
Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
275 280 285  
Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
290 295 300  
Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
305 310 315 320  
Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
325 330 335  
Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
340 345 350  
Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
355 360 365

Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
 385 390 395

<210> 69  
 <211> 439  
 <212> PRT  
 <213> Homo sapiens

<400> 69  
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30  
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
 35 40 45  
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140  
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser

210	215	220
Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe		
225	230	235
Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe		
245	250	255
Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly		
260	265	270
Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly		
275	280	285
Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr		
290	295	300
Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys		
305	310	315
Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile		
325	330	335
Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly		
340	345	350
Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala		
355	360	365
Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn		
370	375	380
Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met		
385	390	395
Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys		
405	410	415
Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala		
420	425	430
Asp Asp Ile Ser Leu Leu Lys		
435		

<210> 70  
 <211> 390  
 <212> PRT  
 <213> Homo sapiens

<400> 70  
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
20 25 30  
Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
35 40 45  
Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
50 55 60  
Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
65 70 75 80  
Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
85 90 95  
Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
100 105 110  
Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
115 120 125  
Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
130 135 140  
Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
145 150 155 160  
Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
165 170 175  
Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
180 185 190  
Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
195 200 205  
Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
210 215 220  
Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
225 230 235 240  
Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
245 250 255  
Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
260 265 270  
Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
275 280 285  
Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
290 295 300  
Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
305 310 315 320

Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
325 330 335  
Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
340 345 350  
Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
355 360 365  
Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
370 375 380  
Ile Pro Gln Thr Asp Glu  
385 390

<210> 71  
<211> 374  
<212> PRT  
<213> Homo sapiens

<400> 71  
Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10 15  
Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
20 25 30  
Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
35 40 45  
Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
50 55 60  
His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
65 70 75 80  
Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
85 90 95  
Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
100 105 110  
Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
115 120 125  
Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
130 135 140  
Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
145 150 155 160  
His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro

165 170 175  
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
180 185 190  
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
195 200 205  
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
210 215 220  
Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
225 230 235 240  
Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
245 250 255  
Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys  
260 265 270  
Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala  
275 280 285  
Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met  
290 295 300  
Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln  
305 310 315 320  
Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
325 330 335  
Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
340 345 350  
Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
355 360 365  
Gly Phe Ala Val Ser Ala  
370

<210> 72  
<211> 14  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> P10-P4'staD-V peptide inhibitor

<221> MOD\_RES  
<222> 10

<223> Xaa is statine moiety

<400> 72

Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe

1 5 10

<210> 73

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> P4-P4' staD-V peptide inhibitor

<221> MOD\_RES

<222> 5

<223> Xaa is statine moiety

<400> 73

Ser Glu Val Asn Xaa Val Ala Glu Phe

1 5

<210> 74

<211> 431

<212> PRT

<213> Homo sapiens

<400> 74

Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Ala

1 5 10 15

Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu

20 25 30

Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly

35 40 45

Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro

50 55 60

Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val

65 70 75 80



Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His  
385 390 395 400  
Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr  
405 410 415  
Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
420 425 430

<210> 75

<211> 361

<212> PRT

<213> Homo sapiens

<400> 75

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
1 5 10 15  
Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
20 25 30  
Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
35 40 45  
Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
50 55 60  
Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
65 70 75 80  
Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
85 90 95  
Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
100 105 110  
Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
115 120 125  
Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
130 135 140  
Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
145 150 155 160  
Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
165 170 175  
Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
180 185 190  
Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn

195	200	205
Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser		
210	215	220
Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe		
225	230	235
Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe		
245	250	255
Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly		
260	265	270
Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly		
275	280	285
Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr		
290	295	300
Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys		
305	310	315
Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile		
325	330	335
Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly		
340	345	350
Phe Ala Val Ser Ala Cys His Val His		
355	360	

<210> 76  
 <211> 63  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(63)  
 <223> n = A,T,C or G

<400> 76  
 garacngayg argarccnga rgarcnngn mgnmgnggnw snttygtnga ratggtnay 60  
 aay 63

<210> 77  
 <211> 21

<212> PRT

<213> Homo sapiens

<400> 77

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val

1

5

10

15

Glu Met Val Asp Asn

20

<210> 78

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Peptide inhibitor P3-P4' XD-V

<221> MOD\_RES

<222> 3

<223> Xaa is hydroxyethylene or statine

<400> 78

Val Met Xaa Val Ala Glu Phe

1

5

<210> 79

<211> 11

<212> PRT

<213> Homo sapiens

<400> 79

Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val

1

5

10

<210> 80

<211> 419

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleotide insert in vector pCF

<400> 80

ctgttggct cgcggtttag gacaaactct tcgcggtctt tccagtactc ttggatcgga 60  
aaccgcgtcg aacctcgaaacg gtactccgac accgagggac ctgagcgagt ccgcacatcgac 120  
cgatcgaa aacctctcgat ctgttgggt gagtactccc tctcaaaagc gggcatgact 180  
tctgcgtaa gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg 240  
gtgatgcctt tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca 300  
agctttaggt gtggcaggct tgagatctgg ccatacactt gagtgacaat gacatccact 360  
ttgcctttctt ctccacaggt gtccactccc aggtccaaact gcaggtcgac tctagaccc 419

<210> 81

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Peptide inhibitor P4-P4' XD-V

<221> MOD\_RES

<222> 4

<223> Xaa is hydroxyethylene or statine

<400> 81

Glu Val Met Xaa Val Ala Glu Phe

1 5

<210> 82

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4' wt

<400> 82

Ser Glu Val Lys Met Asp Ala Glu Phe

1

5

<210> 83

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4'wt

<400> 83

Ser Glu Val Asn Leu Asp Ala Glu Phe

1

5

<210> 84

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 84

Ser Glu Val Lys Leu Asp Ala Glu Phe

1

5

<210> 85

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 85

Ser Glu Val Lys Phe Asp Ala Glu Phe

1

5

<210> 86  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 86  
Ser Glu Val Asn Phe Asp Ala Glu Phe  
1 5

<210> 87  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 87  
Ser Glu Val Lys Met Ala Ala Glu Phe  
1 5

<210> 88  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 88  
Ser Glu Val Asn Leu Ala Ala Glu Phe  
1 5

<210> 89

<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 89  
Ser Glu Val Lys Leu Ala Ala Glu Phe  
1 5

<210> 90  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 90  
Ser Glu Val Lys Met Leu Ala Glu Phe  
1 5

<210> 91  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 91  
Ser Glu Val Asn Leu Leu Ala Glu Phe  
1 5

<210> 92  
<211> 9  
<212> PRT

  
<213> Artificial Sequence

<220>

<223> APP fragment

<400> 92

Ser Glu Val Lys Leu Leu Ala Glu Phe

1

5

<210> 93

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 93

Ser Glu Val Lys Phe Ala Ala Glu Phe

1

5

<210> 94

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 94

Ser Glu Val Asn Phe Ala Ala Glu Phe

1

5

<210> 95

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP fragment

<400> 95

Ser Glu Val Lys Phe Leu Ala Glu Phe

1

5

<210> 96

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

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*10*  
*12*  
*Jan 57*

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Gly Ser Phe Val Glu Met Val Asp Asn Leu

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